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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/510,560	CUMMING ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-39,41,42,47 and 49-109* is/are pending in the application.

4a) Of the above claim(s) *8,9,59,60 and 67-86* is/are withdrawn from consideration.

5)☒ Claim(s) *96 and 97* is/are allowed.

6)☒ Claim(s) *1,3-7,10-39,41,42,47,49-58,61-66,87-95 and 98-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *92305*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

NOTE the change of examiner in this application.

1. The amendment and response filed on 8/8/05 has been fully considered in this application.

2. New claims 87-109 have been added by the amendment filed on 8/8/05.

Election/Restrictions

3. Applicant's election of:

a. low molecular weight heparin (as the drug);

b. sodium caprate (as the salt of a medium chain fatty acid); and

c sodium caprate and halide of caprate (as a single combination of a fatty acid salt and fatty acid acyl derivative); .

in the reply filed on 4/21/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

4. Claims 8-9, 59-60 and 67-86 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

5. This application contains claims 8-9, 67-86 are drawn to an invention nonelected with traverse in Paper filed on 4/21/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Status of the Claims

6. Claims 1, 3-39, 41-42, 47 and 49-86 are currently pending.

7. Claims 8-9, 59-60 and 67-86 are withdrawn from consideration as being directed to a nonelected invention.

8. Claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 and 87-109 are under consideration.

Withdrawn Claim Rejections

9. The rejection of claims 1, 3-6, 10-13, 26-28, 39, 52-57 and 61-66 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284, has been withdrawn in view of the amendment to the claims and response.

10. The rejection of claims 1, 3, 6, 10- 14,16-28,33-39, 41-42, 47, 52-54,57 and 61-66 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Jang WO 84/04674 (12/84), has been withdrawn in view of the response and amendments.

11. Claims 1, 3, 6, 7, 10-14,16-28,33-39, 41-42, 47, 52-54,57-58 and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jang WO 84/04674 (12/84) in view of Einarsson US Pat. No. 5,714,477 (2/98: filed 12/95) and/or Watts.

Maintained Claim Rejections

12. The rejection of claims 1, 3-7, 10-39, 47, 49-58, and 61-66 under 35 U.S.C. 102(a,b) as being anticipated, or in the alternative as prima facie obvious over Watts et al. WO 97/05903 (2/97) is maintained for the reasons of record set forth in the previous office action mailed on 5/18/05.

13. The rejection of claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. WO 97/05903 (2/97). In view of Jang WO 84/04674 (12/84) and/or Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284, is maintained for the reasons of record set forth in the previous office action mailed on 5/18/05.

14. The rejection of claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. WO 97/05903 (2/97) in view of Jang and/or Inamori as applied to claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 above, and further in view of Briskin et al. WO 95/22319 (8/95), is maintained for the reasons of record set forth in the previous office action mailed on 5/18/05.

15. The rejection of claims 1, 3-7, 10-13, 26-28, 39, 52-58 and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284 in view of Einarsson US Pat. No. 5,714,477 (2/98: filed 12/95) and/or Watts, is maintained for the reasons of record set forth in the previous office action mailed on 5/18/05.

New Rejection Necessitated by the Amendment

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 87-95, 98-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Watts et al (WO 97/05903 (2/97)*) and Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284.

Independent claim 88 briefly recites a solid composition comprises a hydrophilic or macromolecular drug, and as an enhancer, a salt of medium chain fatty acid which has carbon chain length from 6-20 carbon atoms.

NOTE in this claim, 'capable of being formed in to a solid oral dosage form for delivery to an intestine' is considered as intended use. And the 'constituents comprising the composition are solid at room temperature' is considered as the use of solid constituents in the preparation of the solid composition,' and is considered as 'product-by-process limitation.'

Watts el al. disclose a drug delivery composition for colonic delivery comprising a drug (e.g. polypeptide and polysaccharide including heparin and low molecular weight heparin(refers to claim 93, 103, 106, 108) (see e.g. page 8), and an absorption promoter (p 24, claim 1). More specifically, Watts el al teach that the absorption promoter comprises a fatty acid or a salt thereof, where the fatty acid has between 6 and 16 carbon atoms, for example capric acid or its (sodium) salt (e.g. se pages 5, 24, claims 1 and 3) which can be used alone or in admixture with a fatty acid derivative (e.g. mono/diglycerides: see pages 5-7) to obtain synergy. Watts el a/.

further teach that the drug can be chosen from insulin, calcitonin, LHRH, buserelin, goserelin, vasopressin, heparin, and more (p 8, 11-12, and p 24, claim 6). Lastly, Watts el a/. teach that the composition is formulated in a capsule (e.g. hard/soft gelatin), tablet, or pellet which is comprised of or coated with a material which is dissolved by the conditions found in the intestines e.g. "rate-controlling" (e.g. sustained release), such as a cellulose ester, HPMC (e.g. see page 9, line14-18) or a methacrylic acid polymer (p 1012, 25, claims 8, and 12-14) for in vivo therapeutic administration to a patient (e.g. see pages 14-15). Watts et al disclose the compositions can be formulated as a hard gelatin capsule, the composition may be liquid or semi-solid depending on the carbon chain length of the fatty acid. Further, the reference teaches that the mixtures of Labrasol with C12, C14 and C16 fatty acids will be semi solid at body temperature. Further, Watts discloses that the preferred fatty acid is capric acid or salt thereof such as sodium caprate (refers to claim 91, 101).

The claimed invention differs from the prior art teachings by reciting solid compositions, constituents comprising the compositions are a solid at room temperature. Watts et al disclose drug delivery compositions comprising a drug (heparin) and a medium chain fatty acid salts as an enhancer and a dispersing agent. Watts et al further teach the precise physical nature of the formulations will depend on the carbon chain length of the fatty acid included. Watts discloses the drug formulations which are semi-solid in capsules. Watts does not teach that the constituents of the formulations are solid at room temperature. However, Inamori et al teach that intestinal absorption of a drug (e.g. an anti-thrombin drug Argatroban) is enhanced by solid oral dosage formulations (tablet/enteric-coated & fast release granules) comprising medium chain fatty acid sodium salts (e.g. capric (C10) acid sodium salt) as an absorption enhancer for patient

administration (e.g. dog/human). The drug and enhancer may be present in solid form in physical admixture (e.g. at room temperature). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the teachings of solid dosage formulations taught by Inamori et al with Watts et al oral formulations, because Inamori et al teach the advantages of use of solid dosage form in the intestinal absorption of the drug.

Regarding the limitation 'salt of medium chain fatty acid is the only enhancer present in the composition', Watts et al teach compositions comprising salts of medium chain fatty acid and a dispersing agent. The dispersing agent in the compositions of Watts et al is considered as additional constituents. And further Inamori et al teach solid oral dosage formulations (tablet/enteric-coated & fast release granules) comprising medium chain fatty acid sodium salts (e.g. capric (C10) acid sodium salt). Thus, it would have been obvious to one skilled in the art to manufacture solid oral dosage formulations comprising drug and salts of medium chain fatty acids as enhancer.

Response to Arguments

19. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

20. Claims 1, 3-7, 10-39, 47, 49-58, and 61-66 are rejected under 35 U.S.C. 102(a,b) as being anticipated, or in the alternative as prima facie obvious over Watts et al. WO 97/05903 (2/97).

Claim 1 (and claims dependent thereon) is drawn to:

A solid oral dosage form comprising :

i. a drug; and

ii. a salt of a medium chain (6-20 carbons) fatty acid (e.g. as an enhancer: preferably capric acid (C10) and its sodium salt: sodium caprate) separately or in combination with fatty acid derivatives. Although the composition requires that "each of said constituents and any other constituent comprising the composition is a solid at room temperature" this limitation is not afforded patentable weight since it refers to the physical state of the intermediates and the use of the intermediates to make the final product. In other word, this limitation defines the ultimate product by its process of manufacture (e.g. dry blending). A product-by-process claim is treated by the PTO as product.

Watts el al. disclose a drug delivery composition for colonic delivery comprising a drug (e.g. polypeptide and polysaccharide including heparin and low molecular weight heparin: see e.g. page 8), and an absorption promoter (p 24, claim 1). More specifically, Watts el al teach that the absorption promoter comprises a fatty acid or a salt thereof, where the fatty acid has between 6 and 16 carbon atoms, for example capric acid or its (sodium) salt (e.g. se pages 5, 24, claims 1 and 3) which can be used alone or in admixture with a fatty acid derivative (e.g. mono/diglycerides: see pages 5-7) to obtain synergy. Watts el a/. further teach that the drug can be chosen from insulin, calcitonin, LHRH, buserelin, goserelin, vasopressin, heparin, and more (p 8, 11-12, and p 24, claim 6). Lastly, Watts el a/. teach that the composition is formulated in a capsule (e.g. hard/soft gelatin), tablet, or pellet which is comprised of or coated with a material which is dissolved by the conditions found in the intestines e.g. "rate-controlling" (e.g. sustained release), such as a cellulose ester, HPMC (e.g. see page 9, line14-18) or a methacrylic acid polymer (p 1012, 25, claims 8, and 12-14) for in vivo therapeutic administration to a patient (e.g. see pages 14-15).

21. Applicant's arguments filed on 8/8/05, regarding the rejection of claims over Watts et al (WO 9705903) have been fully considered but they are not persuasive.

a) Applicants argue that Watts neither teaches nor suggest the composition comprising

constituents, all of which are solid at room temperature and includes a fatty acid salt, nor the preparation of a dosage form which contains, as the only enhancer present in the dosage form, one or more members of the group consisting of fatty acid salt, halide, anhydride glyceride, and difuctional fatty acid derivatives (see response page 23).

Regarding claims 1, 3-7, 10-39, 49-52 applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., dosage form comprising only one enhancer) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 53-58, 61-66 recite that ' as the only enhancer present in the dosage form one or more members selected from the group consisting of ....', which can be interpreted as the "dosage form comprising more than one member of salt of fatty acid which has a carbon chain length of from 6 to 20 carbon atoms.

Further, according to the instant specification, the 'enhancer in a medium fatty acid salt, ester or ether or a derivative of a medium chain fatty acid....', and the specification further teaches 'preferably, the enhancer id a solium salt of medium chain fatty acid, ...most preferably, the enhancer if sodioum caprate (elected species).'

Watts et al use surfactants as suitable'**dispersing agents'**, which would not read on the enhancer of the instant claim dosage forms. And further the instant claim solid dosage form recites 'comprising', which would be open to other reagents such as dispersing agents. Further, the claim recites that 'any other constituents', which may read on the dispersing agent of the

reference. The claimed oral dosage form is interpreted as 'comprising only one enhancer, but open to other reagents such as dispersing agents.' Watts et al teaches only one single enhancer, however teaches the use of 'dispersing agent' along with the only one enhancer used.

b) Applicants argue examiner has explained the legal basis that permits to treat the composition claim as being product-by-process claims.

Applicants traverse Examiner's interpretation of claim limitation "...each of the constituents and any other constituents comprising dosage form are a solid at room temperature.'

Examiner interprets 'this limitation defines ultimate product by its process of manufacture. A product-by-process claim is treated as by the PTO as product' (see previous office action page 3).

Applicants arguments have been fully considered and are not persuasive.

The instant claim 1 recites 'a oral dosage form comprising a hydrophilic or macromolecular drug, and an enhancer....., wherein said dosage from and each of the constituents and any other constituents comprising the dosage form are a solid at room temperature.'

Thus according to the claim limitations the dosage form and the constituents are a solid room temperature.

According to the examiner the solid dosage form is solid at room temperature, and examiner interprets the 'constituents which are used in the manufacture of the final dosage form are considered as the intermediates used in the process of the manufacture of the claimed dosage form. Thus examiner's position is that the 'solid state of the constituents' is not relevant to the claimed final dosage form, as long as the final product 'the oral dosage form' is solid. In this

context examiner has considered the claim limitation 'constituents comprising the dosage form' as the 'product-by-process limitation.'

Watts et al further teach the precise physical nature of the formulations will depend on the carbon chain length of the fatty acid included.

Watts et al disclose the compositions can be formulated as a hard gelatin capsule, the composition may be liquid or semi-solid depending on the carbon chain length of the fatty acid. Further, the reference teaches that the mixtures of Labrasol with C12, C14 and C16 fatty acids will be semi solid at body temperature. Thus, Watts et al teach compositions which are solid at room temperature.

Further, Watts discloses that the preferred fatty acid is capric acid or salt thereof such as sodium caprate (the elected species).

NOTE the newly added limitation 'for delivery to an intestine' is considered as intended use limitation.

Thus, for the reasons of record the rejection is maintained.

22. Claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. WO 97/05903 (2/97). In view of Jang WO 84/04674 (12/84) and/or Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284.

Claim 1 (and claims dependent thereon) is drawn to:

A solid oral dosage form comprising :

i. a drug; and

ii. a salt of a medium chain (6-20 carbons) fatty acid (e.g. as an enhancer: preferably capric acid (C10) and its sodium salt: sodium caprate) separately or in combination with fatty acid derivatives.

Although the composition requires that "each of said constituents and any other constituent comprising the composition is a solid at room temperature" this limitation is not afforded patentable weight since it refers to the physical state of the intermediates and the use of the intermediates to make the final product. In other word, this limitation defines the ultimate product by its process of manufacture (e.g. dry blending). A product-by-process claim is treated by the PTO as product.

Present claim 41 (and dependent claim 42) is drawn to a method of making a solid oral dosage form comprising a blend of room temperature solids of:

i. a drug;

ii. a medium chain (6-20) fatty acid or salt or derivative thereof; and

iii. optional components.

Which is formed into a solid oral dosage form by

i. direct compression of the blend (e.g. to form tablets); or

ii. granulating the blend to form a granulate for incorporation into said dosage form.

Watts el al. disclose a drug delivery composition for colonic delivery comprising a drug (e.g. polypeptide and polysaccharide including heparin and low molecular weight heparin: see e.g. page 8), and an absorption promoter (p 24, claim 1). More specifically, Watts el al teach that the absorption promoter comprises a fatty acid or a salt thereof, where the fatty acid has between 6 and 16 carbon atoms, for example capric acid or its (sodium) salt (e.g. se pages 5, 24, claims 1 and 3) which can be used alone or in admixture with a fatty acid derivative (e.g. mono/diglycerides: see pages 5-7) to obtain synergy. Watts el a/. further teach that the drug can be chosen from insulin, calcitonin, LHRH, buserelin, goserelin, vasopressin, heparin, and more (p 8, 11-12, and p 24, claim 6). Lastly, Watts el a/. teach that the composition is formulated in a capsule (e.g. hard/soft gelatin), tablet, or pellet which is comprised of or coated with a material which is dissolved by the conditions found in the intestines e.g. "rate-controlling" (e.g. sustained release), such as a cellulose ester, HPMC (e.g. see page 9, line14-18) or a

methacrylic acid polymer (p 1012, 25, claims 8, and 12-14) for in vivo therapeutic administration to a patient (e.g. see pages 14-15).

The Watts reference differs from the present invention by failing to teach dry direct compression of its composition components to form tablet or granulates for capsule incorporation (present claims 41 and 42, respectively).

However, the Jang or Inamori reference teachings taken separately or in combination provide motivation to one of ordinary skill in the art to formulate the Watt reference solid dosage oral formulations (e.g. tablets/capsules/pellets) by dry compression to form tablet or granulates for capsule incorporation since these references demonstrate that fatty acids and/or their derivatives achieve favorable intestinal drug absorption upon formation of the oral dosage form utilizing dry component blending.

For example, Jang teaches solid oral dosage forms (e.g. controlled-release dosage forms) formed by dry, direct particle compression (to form multiparticlulates and compressed tablets) of:

i. a drug

ii. organic salts of C11-C28 fatty acids alone or blended with C12-C28 fatty acids and/or C12-C28 fatty acid derivatives (e.g. monalcohols/amides/glycerides and

ii. carbohydrate polymer (e.g. ethyl/propyl celluloses) ;

(see E.g. See abstract ; .pages 4, 6-9; examples; and claims)

which components are solid (e.g. particles) at room temperature.

Similarly, Inamori et al. Teach that intestinal absorption of a drug (e.g. an anti-thrombin-drug Argatroban) is enhanced by solid oral dosage formulation (tablet/enteric-coated & fast release granules) of medium chain fatty acid sodium salts (e.g. capric (C10) acid sodium salt) as an absorption enhancer for patient administration (e.g. dog/human). The drug and enhancer is preferably present in solid form in physical admixture (e.g. at room temperature).

Accordingly, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to formulate the Watt's reference oral dosage formulations using dry solid compression of its ingredients in light of the favorable absorption drug enhancement realized by the Jang and/or Inamori references.

23. Applicant's arguments filed on 8/8/05, regarding the obviousness rejection over Watts, Jang and or Inamori et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection, and state that Watts is directed to liquid or semi-solid form of its compositions.

Applicants arguments have been fully considered and are not persuasive, since applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case, applicants have argued Watts reference alone, whereas the rejection is based on combined teachings of Watts in view of Jang et al and/or Inamori et al.

Applicants argue that there is no suggestion whatsoever of the desirability of combining the teachings of either Inamori or Jang which are directed to solid compositions with the liquid or semi-solid compositions of Watts. The solid formulations of Inamori and the dry, direct compression of Jang are simply incompatible with the liquid or semi-liquid compositions of Watts.

Applicants arguments have been fully considered and are not persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner

recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Watts et al teach compositions that can be formulated as a hard gelatin capsule, the composition may be liquid or semi-solid depending on the carbon chain length of the fatty acid. Further, the reference teaches that the mixtures of Labrasol with C12, C14 and C16 fatty acids will be semi solid at body temperature. And Inamori et al teach solid oral dosage form comprising medium chain fatty acid sodium salts as an enhancer. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use enhancer with different lengths of medium fatty acid chain, such that the formulations are solid in room temperature.

Applicants further argue that Watts is directed to compositions of a drug comprising a mixture of fatty acid having 6 to 16 carbon atoms or salt thereof and dispersing agent, and would not result in composition comprising fatty acid component as sold enhancer present in the formulations. Applicants arguments are not persuasive. Watts et al use surfactants as suitable'**dispersing agents'**, which would not read on the enhancer of the instant claim dosage forms. And further the instant claim solid dosage form recites 'comprising', which would be open to other reagents such as dispersing agents. The claimed oral dosage form is interpreted as 'comprising only one enhancer, but open to other reagents such as dispersing agents.' Watts et al teaches only one single enhancer, however teaches the use of 'dispersing agent' along with the only one enhancer used.

NOTE the newly added limitation 'for delivery to an intestine' is considered as intended use limitation.

Thus, the rejection of record has been maintained.

24. Claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. WO 97/05903 (2/97) in view of Jang and/or Inamori as applied to claims 1, 3-7, 10-39, 41-42, 47, 49-58, and 61-66 above, and further in view of Briskin et al. WO 95/22319 (8/95).

The combined teaching of the Watts reference taken in view of Jang and/or Inamori in the obviousness rejection described above is hereby incorporated by reference in its entirety.

The Watts reference teaching (alone or in combination with Jang and/or Inamori) differ from the elected invention by failing to teach a halogen (e.g. hydbromide/ hydrochloride) salt of sodium caprate as the enhancer.

However, the Watts reference alone (or combined with Jang and/or Inamori) clearly teach the use of any C6-C16 fatty acid or salt thereof but preferably a sodium salt particularly sodium caprate.

In this regard, pharmaceutically acceptable salts e.g. carboxylate salts are known to encompass functionally equivalent cationic alkali/alkaline earth metals such as sodium as well as halogen salts (e.g hydrobromide/hydrochloride). See e.g. Briskin at page 3, especially lines 3-25).

Accordingly, one of ordinary skill in the art would have been motivated to select a different fatty acid salt other than sodium (e.g. for sodium caprate) such as a halogen salt with a reasonable expectation of retaining the intestinal enhancement qualities of the Watt reference oral dosage formulations.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to formulate a pharmaceutically acceptable acid halide salt of the medium chain

fatty acids (e.g. sodium caprate) disclosed in the Watts reference in order to obtain a functionally equivalent enhancers for use in formulating solid oral dosage formulations for drug delivery in accordance with the Watts reference teaching method taken alone or as modified by the Jang and/or Inamori reference teaching(s).

25. Applicant's arguments filed 8/8/05, regarding the obviousness rejection of claims over Watts either with Jang and Inamori, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants argue that the combination of Watts either with Jang and Inamori is insufficient to support an obviousness rejection.

Applicants arguments regarding the combined teachings of Watts, Jang and /or Inamori have discussed supra, which are hereby incorporated by reference in its entirety.

Examiner has used the teachings of Briskin to address the halogen salt of sodium caprate as enhancer.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Watts teach the use of any of C6-C16 fatty acid or salt thereof, and preferably sodium salt, sodium caprate. And Briskin teach the sodium salts. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use halogen salt of sodium caprate.

NOTE the newly added limitation 'for delivery to an intestine' is considered as intended use limitation.

Thus, for the reasons of record the rejections have maintained.

26. Claims 1, 3-7, 10-13, 26-28, 39, 52-58 and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inamori et al., Proc. Int's Symp. Control. Rel. Bioact. Mat. 24th (1997) pages 283-284 in view of Einarsson US Pat. No. 5,714,477 (2/98: filed 12/95) and/or Watts.

Claim 1 (and claims dependent thereon) is drawn to:

A solid oral dosage form comprising :

i. a drug; and

ii. a salt of a medium chain (6-20 carbons) fatty acid (e.g. as an enhancer: preferably capric acid (C10) and its sodium salt: sodium caprate) separately or in combination with fatty acid derivatives.

Although the composition requires that "each of said constituents and any other constituent comprising the composition is a solid at room temperature" this limitation is not afforded patentable weight since it refers to the physical state of the intermediates and the use of the intermediates to make the final product. In other word, this limitation defines the ultimate product by its process of manufacture (e.g. dry blending). A product-by-process claim is treated by the PTO as product.

Inamori et al. Teach that intestinal absorption of a drug (e.g. an anti-thrombin drug Argatroban) is enhanced by solid oral dosage formulation (tablet/enteric-coated & fast release granules) of medium chain fatty acid sodium salts (e.g. capric (C10) acid sodium salt) as an absorption enhancer for patient administration (e.g. dog/human). The drug and enhancer may be present in solid form in physical admixture (e.g. at room temperature).

The Inamori et al. Reference teaching differs from the presently claimed invention by failing to teach enhancing absorption of low molecular weight heparin (e.g. claims 7 and 58) using medium chain fatty acids and/or salts (e.g. capric (C10) acid sodium salt) .

However, Einarsson teach that the formation of solid oral dosage formulations of heparin and its low molecular fragments would be beneficial (e.g. as an alternative to injection with poor absorption: see e.g. col.1, especially lines 35-40) and further teach the use of medium chain (C6-18: especially caprylate and/or caprate) fatty acid derivatives (e.g. glycerides) for making oral dosage formulations. See e.g. col. 3, examples and patent claims.

Similarly, Watts el al. disclose a drug delivery composition for colonic delivery comprising a drug (e.g. polypeptide and polysaccharide including heparin and low molecular weight heparin: see e.g. page 8), and an absorption promoter (p 24, claim 1) the promoter comprising a fatty acid or a salt thereof, where the fatty acid has between 6 and 16 carbon atoms, for example capric acid or its (sodium) salt (e.g. se pages 5, 24, claims 1 and 3) which can be used alone or in admixture with a fatty acid derivative (e.g. mono/diglycerides: see pages 5-7) to obtain synergy.

Accordingly, one of ordinary skill in the art would have been motivated to make solid oral dosage formulations e.g. tablets/enteric-coated and fast release) comprising medium chain fatty acids and/or salts in accordance with the Immari method utilizing heparin and/or its low mw fragments in view of the Einarsson reference teaching that solid oral dosage formulations of heparin or its low mw fragments are desirable and achievable by using medium chain fatty acids (e.g. caprylate/caprate) and derivatives (e.g. glycerides) and/or in view of the Watts reference teaching of making solid oral dosage formulations comprising medium chain fatty acids and their derivatives (e.g. salts/glycerides) for heparin/low mw heparin administration.

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to utilize heparin and/or its fragments as the drug in the Imamori reference method

of making solid oral dosage formulations with a reasonable expectation of achieving favorable intestinal drug absorption.

27. Applicant's arguments filed 8/8/05, regarding the obviousness rejection of claims over Inamori et al Einarsson and Watts et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants argue that in this rejection, the examiner has combined teachings of Watts and Inamori and Einarsson for the limited purpose of suggesting the use of heparin and its low molecular fragments in combination with one or more glycerol esters of at least one fatty acid.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Inamori et al teach solid oral dosage formulations of medium chain fatty acid sodium salts. Einarsson teach the heparin and its low molecular fragments and the use of medium chain fatty acid derivatives for making oral dosage forms. Watts et al teach formulation comprising heparin and fatty acid or salt thereof. Thus, it would have been to one skilled in the art at the time the invention was made to use heparin as a drug in the solid oral dosage formulations taught by Inamori et al.

NOTE the newly added limitation 'for delivery to an intestine' is considered as intended use limitation.

Thus, the rejection of record has been maintained.

Allowable Subject Matter

28. Claims 96-97 are allowed.

Conclusion

29. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

08 November 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER